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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,854	01/13/2004	Bin Ye	7570/80962	8530

7590 08/08/2006

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/755,854	YE ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The response filed on 6/8/06 to the restriction requirement of 5/8/06 has been received. Applicant has elected Group I for examination without traverse.

Claims 1-18 are pending.

Claims 6-12 and 14-18 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 1-5 and 13 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims 2-5 and 13 are rejected because claim 1 recites the term "eosinophil-derived neurotoxin (EDN)" as the sole means of identifying the polypeptide of the claimed method. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. Amending

the claims to specifically and uniquely identify eosinophil-derived neurotoxin (EDN) by a SEQ ID NO can obviate the rejection.

Claim 1 and dependant claims 2-5 and 13 are rejected for being indefinite for reciting "significantly higher". It is not clear from the claims or the specification what is meant by "significantly higher". This renders the claim indefinite because the term "significantly higher" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 1 and dependant claims 2-5 and 13 are rejected because claim 1 recites: "A method of determining whether a human female subject is at increased risk of having ovarian cancer..."; however, the claims do not indicate to what said risk would be compared in order to determine that the risk is "increased".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining whether a first

human female has ovarian cancer comprising obtaining a urine test sample from said first human female, determining the amount of EDN (SEQ ID NO:1) in said urine test sample, comparing the amount of EDN determined in said urine test sample with the amount of EDN in a urine sample from a second human female known to be free of ovarian cancer, and concluding that the first human female has ovarian cancer if the amount of EDN in the urine test sample from said first human female is higher than the amount of EDN in the urine sample from said second human female known to be free of ovarian cancer, does not reasonably provide enablement for a method of determining whether a human female subject *is at increased risk of* having ovarian cancer comprising removing any test biological sample from said human female subject and determining the amount of EDN in said test biological sample, comparing the amount of EDN determined in said test biological sample with the amount in just any control biological sample(s), and concluding that said human female subject has *or is likely to develop* ovarian cancer if the amount of EDN in said test biological sample is higher than in said control biological sample(s). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the

breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are drawn to a method of determining whether a human female subject is at increased risk of having ovarian cancer comprising removing any test biological sample from said human female subject and determining the amount of EDN in said test biological sample, comparing the amount of EDN determined in said test biological sample with the amount in just any control biological sample(s), and concluding that said human female subject has or is likely to develop ovarian cancer if the amount of EDN in said test biological sample is higher than in said control biological sample(s).

The specification teaches a method of determining whether a first human female has ovarian cancer comprising obtaining a urine test sample from said first human female, determining the amount of EDN (SEQ ID NO:1) in said urine test sample, comparing the amount of EDN determined in said urine test sample with the amount of EDN in a urine sample from a second human female known to be free of ovarian cancer, and concluding that the first human female has ovarian cancer if the amount of EDN in the urine test sample from said first human female is higher than the amount of EDN in the urine sample from said second human female known to be free of ovarian cancer (Pages 14-15 and Table 1, in particular). The specification and the art do not demonstrate that the claimed method would predictably determine whether a subject has ovarian cancer by using any sample other than urine. Further, the specification and the art do not demonstrate that the claimed method would predictably determine

whether a subject has ovarian cancer by using any control other than a urine sample from a female known to be free of ovarian cancer. Further, the specification and the art do not demonstrate that the claimed method would predictably determine whether any subject *is at any risk of* developing ovarian cancer.

The state of the prior art dictates that if a molecule such as EDN is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent

acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the protein's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use EDN in any diagnostic setting without undue experimentation.

The level of unpredictability for the detection of any disease is quite high. Neither the specification nor the prior art provide evidence of a universal association between the claimed detection method and every type of sample and every type of control. Further, the level of unpredictability for determining whether a subject is "at increased risk of having cancer" is very high. Neither the specification nor the prior art provide *any* evidence that a method of measuring EDN in any sample from a healthy patient would predictably indicate that said healthy patient is at some risk of *developing* ovarian cancer. A practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such associations. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method of determining whether a human female subject is at increased risk of having ovarian cancer comprising removing any test biological sample from said human female subject and determining

the amount of EDN in said test biological sample, comparing the amount of EDN determined in said test biological sample with the amount in just any control biological sample(s), and concluding that said human female subject has or is likely to develop ovarian cancer if the amount of EDN in said test biological sample is higher than in said control biological sample(s), and Applicant has not enabled said method because it has not been shown that every biological test sample would predictably function in the claimed method of detecting ovarian cancer and it has not been shown that a method comprising measuring EDN in any sample from a healthy patient would predictably indicate that said healthy patient is at some risk of *developing* ovarian cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

Summary

No claim is allowed. Claims 1-5 and 13 are rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching a method of detecting ovarian cancer or a risk of developing ovarian cancer comprising measuring levels of EDN in a sample from a patient. The closest prior art for claims 1-5 and 13 is Gleich et al (US Patent 5,928,883; 7/27/99), which teaches a method of detecting inflammatory bowl disease by measuring EDN levels; however, this reference does not teach or suggest a method of

detecting ovarian cancer or a risk of developing ovarian cancer comprising measuring levels of EDN in a sample from a patient.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

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